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Tetrahedron Letters 46 (2005) 5343–5346

Tetrahedron Letters

Urea and thiourea based efficient colorimetric sensors for oxyanions

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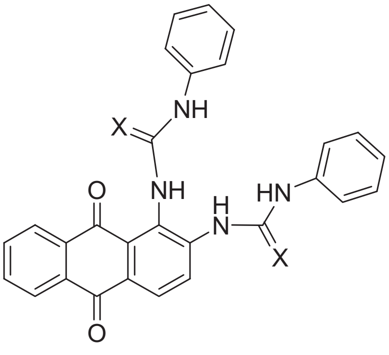
Received 9 February 2005; revised 23 May 2005; accepted 2 June 2005

Abstract—Urea and thiourea based receptors **1** and **2** bind $H_2PO_4^-$, OH^-, $CH_3CO_2^-$, and $PhCO_2^-$ ions in an acetonitrile/DMSO (9:1, v/v) medium. Binding of these anions causes an appreciable change in the visible region of the spectrum, which can be detected by the naked eye. The affinity constant for $H_2PO_4^-$ is higher by about an order of magnitude as compared to the other oxyanions mentioned above. Ab initio calculations predicted tweezer-like binding modes for receptors **1** and **2** with these anions and a higher affinity toward $H_2PO_4^-$ was predicted in acetonitrile.

Anions play a major role in many biological processes and in structures like amino acids, neurotransmitters, enzyme substrates, co-factors, nucleic acids, etc.[1,3] They are also important ingredients for a variety of industries related to agricultural fertilizers, food additives, and water.[2] Along with these, recent emphasis on environmental concerns necessitate the development of highly selective anion sensors.[3] Recently, there has been a considerable surge of interest in developing neutral organic receptor molecules, which are capable of binding specific anionic guests selectively.[4] However, in most cases, the thermodynamic affinity of these receptors for a specific anion analyte has been evaluated either through ^{1}H NMR titration techniques or through analyte binding induced changes in fluorescence or redox potential values. Examples of the selective binding and sensing of anion analytes showing optical output signals are rather limited and are currently being increasingly appreciated; naked eye detection can offer instant qualitative and quantitative information.[5,6] Further a systematic approach to understand the relative affinity of various anions toward a receptor molecule is still at a primitive level. We report herein the binding and relative affinity of several oxyanions, for example, acetate, phosphate, benzoate, and hydroxide toward urea/thiourea derivatives (**1** and **2**) of anthraquinone[5] as receptor molecules in organic solution (Scheme 1). The analyte–receptor binding causes an appreciable change in color in the visible region of the spectrum and thereby allows naked eye detection. Ab initio computed results predicted tweezer-like binding of oxyanions with receptors **1** and **2**. The calculations further suggested the importance of diffuse functions in the basis set and solvent effects in predicting the relative affinity of these oxyanions toward receptor molecules **1** and **2**.



X = O, **1** ; X = s, **2**

Scheme 1. Structures of receptors **1** and **2**.

Receptor molecules **1** and **2** were synthesized following a known procedure.[5] Analytical data (elemental analysis, ^{1}H NMR, and ES-mass spectral studies) match with the formulations of the receptors. Titration experiments of various anions with receptor molecule **1** did not show any color change at room temperature, but a distinct color change was visually noticed when the temperature of the solution was raised to about 60 °C.

Keywords: Oxyanions; Sensor; Urea and thiourea derivatives; Naked eye detection; Ab initio calculation.

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doi:10.1016/j.tetlet.2005.06.011

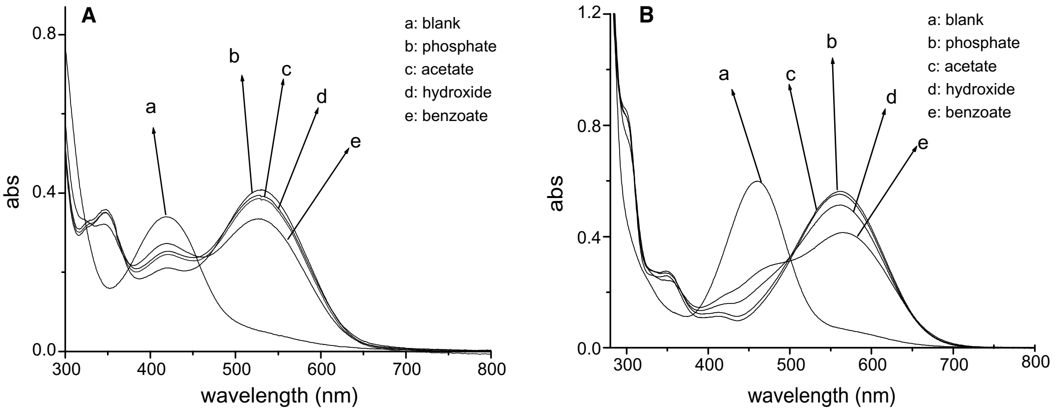

Figure 1. UV–vis changes of (A) receptor **1** at 60 °C (5×10^{-5} M) and (B) receptor **2** at rt (3.3×10^{-5} M) with different oxyanions in DMSO/CH_3CN (1:9, v/v).

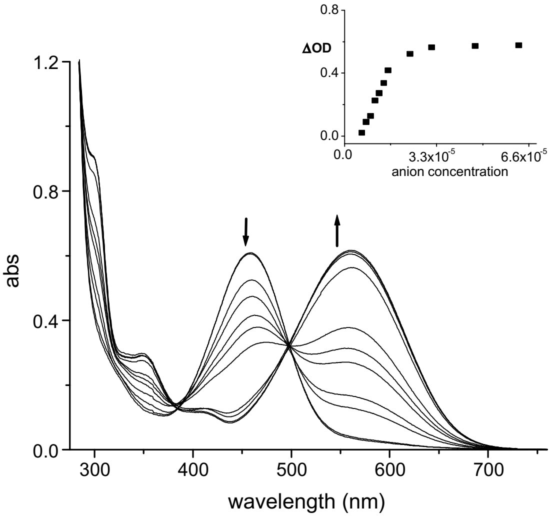

Figure 2. UV–vis changes of receptor **2** (3.3×10^{-5} M) at rt in DMSO/CH_3CN (1:9 v/v) upon addition of phosphate (7.5×10^{-6}–5×10^{-4} M) oxyanion solution. Inset shows the plot of the change in absorbance at 562 nm as a function of anion concentration.

This could be explained by its unfavorable low energy conformation, where various intramolecular hydrogen bonds prevent the bis urea functionality from aligning properly and thereby binding of the respective analyte.[5] The temperature of the DMSO/CH_3CN (1:9 v/v) solution of **1** was raised to 60 °C in the presence of externally added CH_3COO^-/benzoate/$H_2PO_4^-$/OH^-, whereby the color of the solution changed to pale red (Fig. 1A). In contrast, receptor **2** under identical conditions demonstrated an immediate color change from pale yellow to violet at room temperature (Fig. 1B).

A significant bathochromic shift (>100 nm) was observed in all cases for the absorption bands in the visible region for receptors **1** and **2**, respectively (Figs. 1 and 2). This could be explained based on the charge-transfer interaction between the electron rich urea/thiourea-bound anion and the electron deficient anthraquinone moiety. A Job plot for receptor **1** at 60 °C and receptor **2** at rt for the anions studied in a DMSO/CH_3CN (1:9 v/v) solution, showed a maximum at a mole fraction of 0.5 in each case; the titration curve for phosphate with receptor **2** is shown in Figure 2. This signified the formation of a 1:1 complex between the receptor molecule and the various anions studied. This also showed that for both receptor molecules, two urea/thiourea functionalities simply acted as cooperative binding sites. Binding of the anions studied to the respective receptor molecules **1** and **2** was also evident in the ^1H NMR titration experiments in DMSO (d_6). ^1H NMR spectra for receptors **1** and **2**, in the absence and presence of phosphate and acetate ions are shown in Figure 3. The –NH protons disappeared on addition of excess (>5 mol equiv) of the respective anions (Fig. 3). Signals at 9.719 (1H, s) and 9.80 (1H, s) ppm for receptor **1** (at 60 °C) and

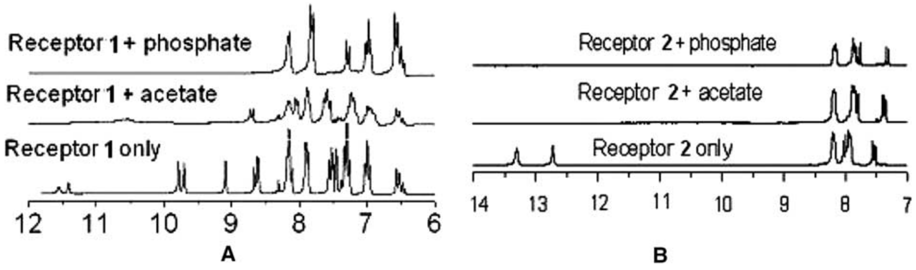

Figure 3. Partial ^1H NMR (200 MHz) of (A) receptor **1** in DMSO-d_6 with 5 equiv of acetate and phosphate ions at 60 °C, (B) receptor **2** in DMSO-d_6 with 5 equiv of acetate and phosphate ions at rt.

Table 1. Association constants for various anions toward receptors **1** and **2**[a,b]

Anion	K_1 (M^{-1})	K_2 (M^{-1})
Acetate	$(7.9 \pm 0.3)10^3$	$(1.5 \pm 0.1)10^5$
Phosphate	$(1.3 \pm 0.1)10^4$	$(1.0 \pm 0.05)10^6$
Benzoate	$(1.3 \pm 0.06)10^3$	$(2.2 \pm 0.04)10^5$
OH^-	$(3.4 \pm 0.07)10^3$	$(4.8 \pm 0.05)10^5$

[a] *tert*-Butyl salts of the respective anions were used for the studies.

[b] K value reported (K_1 for receptor **1** and K_2 for receptor **2**), is the average of the 11 independent data evaluated from each individual UV–vis titration for the respective receptor and anion. Confidence limits for the respective K values are also shown.

12.74 (2H, s) and 13.30 (2H, s) ppm for receptor **2** (at rt), respectively, disappeared on association with various anions. However, addition of excess water to the receptor–analyte complex solution (DMSO/CH_3CN, 1:9 v/v) caused the UV–vis spectra to revert back to the original spectra of **1** or **2**, that is, with λ_{max} at 422 nm for receptor **1** and at 459 nm for receptor **2** with bleaching of the λ_{max} attributed to the corresponding receptor–analyte complexes along with the expected decrease in absorption intensity values due to the dilution effect. This suggests that there was competitive hydrogen bond formation between the –NH protons of the urea/thiourea-functionalities and H_2O molecules with the various externally added anions. To confirm this, similar experiments were performed with D_2O, where less significant changes were observed. These experiments also demonstrated that receptors **1** and **2** bind to the various anions reversibly in organic solvents. Association constants for each individual anion toward respective receptors **1** and **2**, were evaluated based on the UV–vis titration data and are presented in Table 1.

The ab initio calculations performed[6i,7] at the RHF/6-31G* level predicted high binding affinity for receptors **1** and **2** with hydroxyl ions. The binding energies of receptor **1** in the gas phase for OH^-, $CH_3CO_2^-$, and $H_2PO_4^-$ were −92.0, −54.1, and −48.5 kcal/mol, respectively. For receptor **2** the binding energies were −94.8, −54.1, and −49.2, respectively (Table 2). Single point calculations performed at the RHF/6-31+G* level using RHF/6-31G* geometries showed similar trends in selectivity, however, the binding energies were less than those at the RHF/6-31G* level (Table 2). These values further reduced on performing the calculations in acetonitrile using a polarizable continuum model (PCM) at RHF/6-31G*.[8] Solvent phase calculations at the RHF/6-31+G* level in acetonitrile predicted a higher affinity of receptors **1** and **2** toward phosphate ions in agreement

Table 2. Calculated interaction energies for receptors **1** and **2**-anion complexes in kcal/mol[a]

1	Basis set	OH^-	$CH_3CO_2^-$	$H_2PO_4^-$	2	OH^-	$CH_3CO_2^-$	$H_2PO_4^-$
	RHF/6-31G*	−92.0	−54.1	−48.5		−94.8	−54.1	−49.2
		(−26.8)	(−13.1)	(−18.6)		(−30.0)	(−14.7)	(−16.4)
	RHF/631+G*//RHF/6-31G*	−70.6	−47.6	−44.9		−71.6	−46.1	−45.2
		(−5.3)	(−5.0)	(−14.7)		(−6.7)	(−5.9)	(−12.0)

[a] Energies calculated in acetonitrile are given in parentheses.

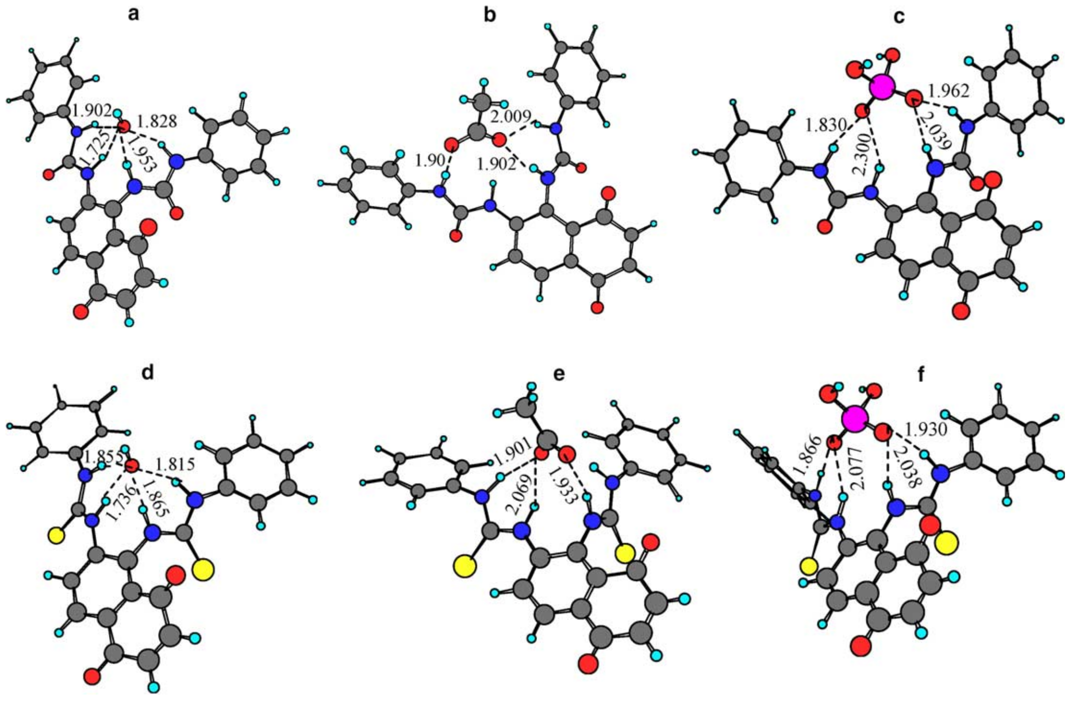

Figure 4. RHF/6-31G* optimized geometries for complexes of receptor **1** with OH^- (a), $CH_3CO_2^-$ (b), and $H_2PO_4^-$ (c) and for complexes of receptor **2** with OH^- (d), $CH_3CO_2^-$ (e), and $H_2PO_4^-$ (f) (color key: red = oxygen, blue = nitrogen, yellow = sulfur, purple = phosphorus).

with the experimental observation (Tables 1 and 2). The benzoate ion was not considered for calculations due to its size. Since ionic hydrogen bond strength is dependent on solvent polarity, the calculated binding energies were greatly reduced in polar solvents. The calculated structures of receptors **1** and **2** with OH^-, $CH_3CO_2^-$, and $H_2PO_4^-$ anions demonstrated a quite interesting feature of these bindings. As shown in Figure 4, tweezer-like binding modes for receptors **1** and **2** with these anions were observed. Hydroxyl anions being smaller in size, interact more strongly with receptors **1** and **2**. All four N–H hydrogens participate in H-bonding with the hydroxide anions (Fig. 4). $H_2PO_4^-$ oxygens also hydrogen-bond with all four N–H hydrogens. However, acetate anions take advantage of only three N–H hydrogens for H-bonding with receptors **1** and **2** (Fig. 4). Therefore, the better fit of hydroxyl ions with **1** and **2** leads to larger binding energies than those of acetate and phosphate ions in the gas phase.

These preferences, however, change in acetonitrile incorporating diffuse functions in the basis set and $H_2PO_4^-$ was found to be energetically preferred over OH^- and $CH_3CO_2^-$ (Table 2).[8] The importance of diffuse functions in anion calculations has been succinctly reviewed by Chandrasekhar et al.[9] Recently, Kameta and Hiratani have shown the recognition of phosphate anions by a boron complex having multiple hydrogen bonding sites.[10] Interestingly, our simple receptors **1** and **2** show even larger stability constants with phosphate anions.

In conclusion, we have shown that receptors **1** and **2** effectively and selectively recognize biologically important $H_2PO_4^-$ ions over other oxyanions such as OH^-, $CH_3CO_2^-$, and $PhCO_2^-$ in acetonitrile. Ab initio calculations predicted tweezer-like binding modes for receptors **1** and **2** with these anions and in contrast to the gas phase selectivity for OH^- ions, the selectivity for $H_2PO_4^-$, as observed in our experimental observations, was qualitatively reproduced in acetonitrile.

Acknowledgements

The authors A.D. and B.G. thank DST (New Delhi) for financial support. D.A.J. and D.K.K. acknowledge CSIR, India, for Senior Research Fellowships.

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